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REMARKS

Support for the Amendment to claim 31 can be found, for example, at the bottom of page 5 of the specification.

Thus, entry of the amendments, which raise no issue of new matter, is requested respectfully.

I. Regarding the Election of Species requirement, Applicant respectfully requests that the Election be reconsidered.

In the Action, the Examiner posited that claims 50-53 do not recite activating NK cells.

However, the properties of a product are inherent therein. Activating NK cells is a property of the claimed Hsp70 protein. Thus, the issue is not believed to be a proper basis to ground the Election.

The Examiner referred to the cited art. In Multhoff et al., J. Imm, page 4341, sentence bridging the columns, the reference teaches that Hsp70 is associated with autoimmunity, pathogen-induced inflammation and cancer. U.S. Pat. No. 6,261,839, column 2, third full paragraph teaches that NK cells are active against cancer and infectious diseases. WO97/10001 is entitled, "Treatment or Prevention of Neoplastic and Infectious Diseases with Heat Shock/Stress Proteins."

Thus, the cited art recognizes a commonality of activity by Hsp70 and NK cells.

Finally, the art recognizes the cytotoxicity targets of NK cells.

Therefore, it is requested respectfully to collapse the Election.

II. Regarding Item 4, the Examiner objected to the claims and stated that the enumerated dependent claims fail to limit the subject matter of the previous claims from which they depend.

The objection is traversed for the following reasons.

With respect to claim 37, the claim has been amended to read as a multiple dependent claim.

Regarding claim 43, because claim 37 has been corrected to be a multiple dependent claim, claim 42 is not dependent solely on the subject matter of claim 36.

With respect to claim 53, there is no explanation in the Office Action of an objection thereto and the claim appears proper.

In view of the amendment and arguments, withdrawal of the objection is in order.

III. Regarding item 6, the Examiner alleged, under 35 U.S.C. §112, second paragraph, indefiniteness of claims 30-42, 44-48 and 50-60.

The rejection is traversed for the following reasons.

The Examiner asserted that claim 53 does not clearly modify the characteristics of the composition, focusing on the term "recombinant."

The word "recombinant", is well recognized to one of skill in the art, and connotes e.g., the extent of glycosylation, ability to comprise fusion proteins, ease of purification,

effects on solubility etc. As such, one of skill in the art would recognize the metes and bounds of the term, and thus, its use in modifying the characteristics of the composition.

Regarding the word "derivative," the term is defined on page 3, three lines up from the bottom, to page 4, line 4.

Accordingly, the claims are definite and distinct. Withdrawal of the rejection is in order.

IV. With respect to Item 8, the Examiner, under 35 U.S.C. §112, first paragraph, asserted that only incubation of cells *ex vivo* leading to activation of NK cells is supported by the specification, and thus temporal elements applied to administration are not.

The rejection is traversed for the following reasons.

Page 9, lines 1 and 2 discloses:

> "If the NK cells are administered before Hsp70 proteins, the corresponding time period before administration of the HSP70 should be at least 3-24 hours."

Thus, there is support for temporal administration features.

The Examiner raised an issue of the derivatives where it is unclear whether the issue relates to written description or enablement.

The Examiner focused on the "multitude of species" allegedly encompassed by the claim(s). Such an argument is one sounding as to scope, thus enablement.

The derivatives of interest have a particular function, namely, activating NK cells.

Accordingly, the specification clearly teaches the claimed invention. One of skill in the art would clearly know so on reading the instant specification. Hence, the rejection has been overcome.

V. Claims 50-53, 54, 56 and 58-60 stand rejected under §102(b) as being anticipated by Srivastava. The Examiner asserted that the reference discloses a method to induce an immune response by administering a composition comprising immune modifiers or antigenic molecules in combination with an Hsp.

The rejection is traversed for the following reasons.

Srivastava teaches at page 3, lines 13-15 that Hsp70 elicited immunity to the tumor from which it was isolated but not to antigenically distinct tumor cells.

The instant specification expressly teaches the contrary (see e.g., at page 4, line 21, MHC compatibility).

Further, the SUMMARY OF INVENTION of Srivastava expressly recites administering a composition of a complex consisting of Hsp and an antigenic molecule. Moreover, the complex must consist essentially of these components.

The instant invention adds no such complex. In fact, the instant specification teaches that complexes as envisioned by the state of the art were disadvantageous (see page 2, lines 1-17 of the instant specification). Further, given that the present invention is not dependent on the MHC type (antigenicity) of the tumor cells, while that of Srivastava is dependent on MHC, the compositions are in fact different.

Hence, Srivastava does not anticipate the claimed invention and the rejection can be removed.

VI. Claims 31-36 stand rejected under §102(b) as being anticipated by Multhoff et al (J Immunol). The Examiner asserted that the reference discloses a method for ex vivo activation of NK cells (i.e., anticipating claim 31) and meets the elements as recited in claims 32-36.

The rejection is traversed for the following reasons.

The method of Multhoff et al. requires the use of membrane bound Hsp.

The instant invention uses a free/isolated peptide, protein or fragment.

Hence, anticipation does not lie and the rejection can be removed.

VII. Claims 31-37 and 39-41 stand rejected under §102(b) as being anticipated by Multhoff et al. (Blood).

Again, the Examiner asserted that the reference discloses a method for ex vivo activation of NK cells which meets the elements as recited in rejected claims.

The rejection is traversed for the following reasons.

Multhoff et al. (Blood) demonstrate that the method requires the use of membrane bound Hsp.

The instant invention uses a free/isolated peptide, protein or fragment.

Accordingly, the rejection must be removed.

VIII. Claims 31-37, 39-41, 50-56 and 58-60 stand rejected under §102(e) as being anticipated by Multhoff et al (U.S. Serial No. 6,261,839).

The rejection is traversed for the following reasons.

The '839 patent teaches treating NK cells with heat and then with a lysosphingolipid or edelfosine.

On the other hand, the instant invention relates to exposing NK cells to isolated Hsp70.

Thus, the '839 patent does not teach the claimed invention and so the rejection can be removed.

IX. Claims 31-37, 39-42, 43, 48, 50-53 and 58-60 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Multhoff et al. (Blood) in view of what is suggested in Multhoff et al. (not clear which reference is being cited from the Action) and Srivastava.

The Examiner asserted that based on the disclosures as outlined in the anticipation rejections, Multhoff et al. fail to teach concurrent or subsequent administration of a Hsp70 protein in addition to the activated cells. The Examiner then went on to suggest that it would have been obvious to administer such cells with Hsp70. Further, it is suggested that it would be obvious to exchange Hsp70 for Hsp72 using a particular reading of the case law.

The rejection is traversed for the following reasons.

There is no teaching of the invention as claimed as argued above. Thus, there is no teaching or suggestion of using purified/isolated Hsp70. Instead, the cited references teach complexes and membrane bound constituents.

The use of Hsp72 for Hsp70 does not achieve the invention as claimed.

Also, the facts of the instant invention are distinguished from those of *In re Kerkhoven*. In the case cited, there was no difference between the components as described in the art and the components as recited in the claims. As provided above, the instant invention uses free protein and the protein of the prior art is either complexed or membrane bound.

There is no teaching or suggestion of substituting isolated Hsp70 for membrane-bound Hsp70 or complexed Hsp70. Moreover, there is no reasonable expectation that such an alleged substitution would lead to tangible results as those claimed.

Also, because the cited references teach complexes or membrane-bound Hsp70, there is no suggestion than an isolated component thereof would be operable. Instead, the cited references teach away from the claimed invention. Clearly, an artisan would expect that the complex or auxiliary molecules associated with Hsp70 would be required for the NK cell activation.

Hence, there is no suggestion for the claimed invention and a prima facie case of obviousness has not been made. Accordingly, the rejection can be removed.

X. Claims 31-36 stand rejected under the judicially-created doctrine of

obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Pat. No. 6,261,839 ('839).

The Examiner asserted that the rejected claims would be anticipated by the claims of the cited patent.

The rejection is traversed for the following reasons.

The Examiner has not met the burden necessary to establish obviousness-type double patenting because neither 1) the differences between the inventions defined by the conflicting claims (claim in the patent compared to a claim in the application) nor 2) the reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent were recited (See MPEP §804 II, C.1.). The Examiner alleged that the reference as anticipates the claims, the rejection is defective.

In any event, as argued above, the '839 patent does not anticipate the claimed invention.

Moreover, there is no suggestion to use isolated Hsp70.

Thus, a prima facie case of obviousness has not been made. Accordingly, the rejection can be removed.

CONCLUSION

Applicant submits that the pending claims are in condition for allowance. Reexamination, reconsideration, withdrawal of the objections and rejections, and early indication of allowance are requested respectfully. If any questions remain, the Examiner is urged to contact the undersigned at the local exchange noted below.

If any fees are found to be applicable, please charge any additional fees or make any credits to Deposit Account No. 07-1896.

Respectfully submitted,

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